REMARKS

Claims 33-53 are pending in this application.

DRAWINGS

Replacement Sheets

Applicant's proposed corrections of sheets 2/49, 5/49 and 7/49 filed 8/2/04 were approved by the Examiner in the Office action dated October 25, 2004. In accordance with the Examiner's request, Applicants hereby submit formal drawing sheets 2/49, 5/49 and 7/49 **marked "Replacement Sheet"** in accordance with 37 CFR 1.84(c). Replacement Sheet 2/49 which includes Fig. 1G, replaces the original sheet 2/49. Replacement Sheet 5/49 which includes Figs. 2A and 2B, replaces the original sheet 5/49. Replacement Sheet 7/49 which includes Fig 3C, replaces the original sheet 7/49.

Objection under 37 C.F.R. §1.83(a)

The drawings were objected to under 37 C.F.R. §1.83(a), which states in part "the drawing in a nonprovisional application must show every feature of the invention specified in the claims". The Examiner states that a single drawing is required showing an "apparatus for **analysis of a plurality of biochips** comprising a plurality of **stations**, a plurality of **thermocontrollers**, a plurality of **interconnects** illustrated as claimed, a **signal generator**, and a **detector** (Office action dated October 25, 2004 at page 2 (emphasis added)).

The Applicants respectfully disagree that a new drawing showing every feature of the invention specified in the claims is required. As stated in 35 U.S.C. §113, "applicant shall furnish a drawing where necessary for the understanding of the subject matter sought to be patented" (emphasis added). Applicant's submit that a new drawing is not necessary under 35 U.S.C. §113 because the specification provides sufficient basis for understanding the

subject matter sought to be patented. The application is directed to devices and methods that allow for simultaneous multiple biochip analysis. The devices are configured to hold multiple cartridge stations comprising multiple biochips that allow high throughput analysis of samples. Clearly, the system requires a signal generator, a detector, and appropriate interconnects to allow electronic detection.

One skilled in the art would understand that the specification provides sufficient basis for understanding the subject matter sought to be patented. Specifically, the first paragraph of the Detailed Description describes "devices designed to receive and **analyze a plurality of biochips**", comprising "a number of cartridge **stations**" which can include "**thermocontrollers**", "**signaling systems**" and "**detectors**" (specification at page 11, lines 25-34). The specification also describes that each station can have a number of different functional components, including, but not limited to, **interconnects** to electronic components, thermocontrollers, signaling systems (specification at page 87-88; lines 36-3).

The Applicants submit that a drawing would not add to the robust discussion of the invention, the claimed subject matter is easily understood by the description. Clearly the specification as filed provides sufficient basis for understanding the subject matter sought to be patented and a drawing is not necessary under 35 U.S.C. §113 for understanding the subject matter.

In view of the forgoing remarks, Applicant's respectfully request reconsideration and withdrawal of the objection.

Rejection Under 35 U.S.C. §112, first paragraph

Claims 33-53 stand rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement. The Examiner asserts that the claims contain subject matter which was not described in the specification in such a way as to reasonably

convey to one skilled in the art that the inventors, at the time the application was filed, had possession of the claimed invention. Applicants respectfully traverse.

Applicant's respectfully assert that Examiner has the initial burden of presenting evidence or reasons why persons skilled in the art would not recognize in an applicant's disclosure a description of the invention defined by the claims. *In re* Wertheim 541 F.2d 257, 265 (CCPA 1976); see also Ex parte Sorenson, 3 USPQ2d 1462, 1463 (Bd. Pat. App. & Inter. 1987). Applicant's respectfully submit that the Examiner failed meet the initial burden of presenting evidence or reasons why persons skilled in the art would not recognize in Applicant's disclosure a description of the invention defined by the claims.

Even assuming, *arguendo*, that the Examiner has met this burden, Applicant's submit that each of the pending claims 33-53 is supported by the specification and claims as originally filed. The application is directed to devices and methods that allow for simultaneous multiple biochip analysis. The devices are configured to hold multiple cartridge stations comprising multiple biochips that allow high throughput analysis of samples. Exemplarily sections of the specification where specific support can be found for Claims 33-53 are detailed in the chart below.

Claim No.	Support (page:line)
33	**<u>multiplexers</u>** "The present invention is directed to devices designed to receive and analyze a plurality of biochips, each comprising an array of biological moieties, such as nucleic acids or proteins, to allow high throughput analysis and detection of target analytes in samples. Thus for example a number of samples (particularly patient samples) can be simultaneously analyzed, or multiple assays can be run on a single sample. The devices comprise a number of cartridge stations that are configured to receive the biochips, with different types of biochips allowing different types of components. The stations can include a wide variety of different components, including thermocontrollers, signaling systems, sensors for leak detection, alphanumeric displays, and detectors. Preferred embodiments include the use of biochips comprising electrodes that rely on electrochemical detection, and thus the devices and/or stations can comprise device boards and processors." **(Page 11, lines 25-34);**

	"Accordingly, the present invention provides biochips, with covalently attached capture binding ligands (e.g. capture probes). The biochips are incorporated into the cartridges of the invention and then fitted into the stations of the multiplexing devices of the invention for running assays. In a preferred embodiment, the biochips are attached to the rest of the cartridge in a wide variety of ways. In one embodiment, the biochip is made directly on a portion of the cartridge and is thus incorporated into the system. Alternatively, as outlined herein, when the biochip is formulated on a different substrate than the remainder of the cartridge, there are a variety of attachment mechanisms that can be used, depending on the composition and configuration of the two substrates." **(Pages 85-86:lines 32-3);** "In Figure 71, there is illustrated a schematic block diagram of an exemplary signal processing approach. A digital to analog converter (DAC) receives a digital signal from a signal source (such as signal generating circuitry on the signal processing printed circuit board or received from a connected personal computer) and converts that signal into an analog signal which is received by filter. The characteristics of filter may be modified to provide frequency low-pass, high-pass, or single or multiple band-pass characteristics according to tailored the signal applied to the electrodes of the E-Chem Cell. In this embodiment, the filtered signal is passed through resistor R9 (110 Kohm) before passing through a first auxiliary amplifier (AUX AMP). To reduce signal complexity and cost, the signal is desirably multiplexed through multiplexer (MUX) and distributed to a plurality of auxiliary electrodes on the E-Chem cell cartridge. A set of reference electrodes is also disposed within the E-Chem Cell cartridge, the outputs of which are coupled to through a second multiplexer (MUX) and reference amplifier (REF AMP) and resistor R13 (110 Kohm) back to the input of first auxiliary amplifier. Finally, a set of active electrodes (36 active electrodes in this embodiment) are coupled via printed circuit board traces to a third mutiplexer. The output of this active electrode multiplexer is amplified by an input signal amplifier (INPUT AMP), and after further optional signal conditioning (such as filtering, gain control and/or selection) is processed through a buffer amplifier (BUFFER AMP) and converted from analog to digital (ADC) form, so that it may be communicated, processed, analyzed, stored or the like in digital form. In Figure 72 there is illustrated an embodiment of a Thermal Control Block Diagram. A microprocessor communicates with an external signal source or sink via a serial communication channel or link. Advantageously, microprocessor generates a control signal to provide an indication of an ON, OFF, or FLASH status to an LED logic circuit which is coupled with and causes LED Drivers to send signals to each of six slots causing each of the slots red or green lights to be on, off, or flash. Microprocessor also generates a signal to DAC. This signal is amplified to power a heat sink blower to control the temperature of the heat sink. A heat sink temperature sensor is associated with

	the heat sink and this sensor generates a temperature signal which is fed back to the microprocessor in feedback manner to control operation or non-operation of the heat sink blower motor. The microprocessor also generates a plurality of signals which are received by a plurality of DAC and driver amplifiers to a Peltier thermal block for each slot. A temperature sensor is also associated with each Peltier thermal block to provide a sensed temperature indication back to the microprocessor for controlling the Peltier thermal block drive signal in feedback manner. In Figure 73 there is illustrated an exemplary layout for a signal processing printed circuit board. Each board includes an edge connector for coupling with a communication bus, motherboard, or other interconnect as are known in the art. Each board in this particular embodiment further includes pad selector circuitry, memory, a CPU/lock-in amplifier, buffers, serial communication circuitry, waveform signal generators, analog-to-digital converter (ADC), filters or filter circuits, master gain circuit, current-to-voltage converter, power regulators, and chip selector (ref/mux)." **(Pages 10-11, lines 16-21);** **<u>thermocontrollers</u>** The microprocessor also generates a plurality of signals which are received by a plurality of DAC and driver amplifiers to a Peltier thermal block for each slot. A temperature sensor is also associated with each Peltier thermal block to provide a sensed temperature indication back to the microprocessor for controlling the Peltier thermal block drive signal in feedback manner. **(Page 11, lines 11-14)** "In a preferred embodiment, when the cartridge comprises a biochip that relies on electrodes for detection, the stations comprise matching interconnects for the biochip, to allow electronic communication between the chip and the device. In a preferred embodiment, each station comprises an individual thermal controller. "Thermal controller" or "thermocontroller" in this context includes elements that can both heat and cool the cartridges and thus the samples in the cartridges as well. In general, given the size and function of the systems, it is desirable to utilize small, fast thermocontrollers. There are a wide variety of known suitable thermocontrollers, including Peltier systems. In general, the thermocontroller should be able to heat/cool samples ranging from 0 to about 100°C and at a rate ranging from 0.01°C/sec to 10°C/sec. It should be noted that a thermocontroller can be used after an assay to destroy the biological material in the cartridge. That is, it is frequently desirable to minimize the exposure of health care workers and lab workers to potentially dangerous samples, and to facilitate the disposal of these materials. The thermocontroller can be used to heat the spent sample at extreme temperatures for some period of time in order to kill or destroy the sample. In addition, heating in conjunction with the addition of other generally harsh reagents (strong acid, strong base, etc.) can also be used. Furthermore, in some embodiments, an

	RF antennae is used to generate plasma that is pumped into the chamber after fluid evacuation to destroy all biological material. In one embodiment, rather than each station comprising an individual thermal controller, sets (for example, rows or columns) of the stations share a thermal controller. In an alternative embodiment, the multiplexing device comprises a single thermal controller."**(Page 87, lines 4-29)**; **Figures 71-73**
34	"Detection of electron transfer, i.e. the presence of the ETMs, is generally initiated electronically, with voltage being preferred. A potential is applied to the assay complex. Precise control and variations in the applied potential can be via a potentiostat and either a three electrode system (one reference, one sample (or working) and one counter electrode) or a two electrode system (one sample and one counter electrode). This allows matching of applied potential to peak potential of the system which depends in part on the choice of ETMs and in part on the other system components, the composition and integrity of the monolayer, and what type of reference electrode is used."**(Pages 93-94, lines 35-4);** **Pages 10-11, lines 16-21 (above);** **Figures 71-73**
35	"The device for measuring electron transfer amperometrically involves sensitive current detection and includes a means of controlling the voltage potential, usually a potentiostat. This voltage is optimized with reference to the potential of the electron donating complex on the label probe." **(Page 96, lines: 13-17)**; **Pages 10-11, lines 16-21 (above);** **Figures 71-73**
36	"Detection of electron transfer, i.e. the presence of the ETMs, is generally initiated electronically, with voltage being preferred. A potential is applied to the assay complex. Precise control and variations in the applied potential can be via a potentiostat and either a three electrode system (one reference, one sample (or working) and one counter electrode) or a two electrode system (one sample and one counter electrode). This allows matching of applied potential to peak potential of the system which depends in part on the choice of ETMs and in part on the other system components, the composition and integrity of the monolayer, and what type of reference electrode is used. As described herein, ferrocene is a preferred ETM. **(Pages 93-94, lines 36-4);** **Pages 10-11, lines 16-21 (above);** **Figures 71-73**
37	"When the biochips comprise electrodes, there are a variety of additional components in addition to the chemistry outlined below, which may be present on the chip, including, but not limited to, interconnects, multiplexers, relay devices, filters, RF antennae, heating elements, electromagnetic components, etc. Each electrode comprises an independent lead (interconnect) to transmit input

	and electronic response signals for each electrode of the array. In contrast to previous systems which require the ability to independently alter only input signals to each electrode but not electronic response signals, it is important in the present invention that both input and electronic response signals be independently monitorable for each electrode. For a relatively small number of electrode pads and/or depending on the desired size of the array, providing direct connections using parallel circuits may be appropriate. In a preferred embodiment, each electrode is individually connected to a corresponding input of a multiplexer via a corresponding interconnector. One problem presented in conventional systems and methods is the difficulty in providing electrical connections (inputs and/or outputs) to a large number of electrodes, particularly if the electrodes form a dense or close packed array. Several solutions to this problem have been identified, and include the use of circuitry that allows signal processing either simultaneously as sets of parallel circuits and connections, line-sample array addressing, serially in a time-domain multiplexed manner, or in parallel or serially using frequency domain and/or time-domain based separation techniques, among other available techniques, as are outlined herein. For example, a preferred method to connect a first multiplicity of circuits or lines on the chip to a smaller plurality of lines at a connector leading from the chip are to use a switching device such as a multiplexer (MUX) or relays to selectively couple circuits on the chip or board with circuits off the board. The number of multiplexers will depend on the number of electrodes in the array. In one embodiment, a single MUX is utilized. In a preferred embodiment, a plurality of MUXs are used. This can be done in a variety of ways, as will be appreciated by those in the art; in one embodiment, "sectors" of electrodes are assigned to a particular MUX; thus for example, rows or columns of the array may each have their own MUX. Alternatively, submultiplexers are used; for example, a column or row is connected to a respective sub-multiplexer, with the sub-multiplexer outputs going to another submultiplexer." **(Page 34-35, lines 5-2);** **Pages 10-11, lines 16-21 (above);** **Figures 71-73**
38	**Page 34-35, lines 5-2 (above);** **Pages 10-11, lines 16-21 (above);** **Figures 71-73**
39	**Page 34-35, lines 5-2 (above);** **Pages 10-11, lines 16-21 (above);** **Figures 71-73**
40	"There are a variety of techniques that can be used to increase the signal, decrease the noise, or make the signal more obvious or detectable in a background of noise. That is, any technique that can serve to better identify a signal in the background noise may find use in the present invention. These

	techniques are generally classified in three ways: (1) variations in the type or methods of applying the initiation signals (i.e. varying the "input" to maximize or identify the sample signal); (2) data processing, i.e. techniques used on the "output" signals to maximize or identify the sample signal; and (3) variations in the assay itself, i.e. to the electrode surface or to the components of the system, that allow for better identification of the sample signal. Thus, for example, suitable "input" AC methods include, but are not limited to, using multiple frequencies; increasing the AC amplitude; the use of square wave ACV; the use of special or complicated waveforms; etc. Similarly, suitable "output" AC techniques include, but are not limited to, monitoring higher harmonic frequencies; phase analysis or filters; background subtration techniques (including but not limited to impedance analysis and the use of signal recognition or peak recognition techniques); digital filtering techniques; bandwidth narrowing techniques (including lock-in detection schemes particularly digital lock in); Fast Fourier Transform (FFT) methods; correlation and/or convolution techniques; signal averaging; spectral analysis; etc. Additionally, varying components of the assay can be done to result in the sample signal and the noise signal being altered in a non-parallel fashion; that is, the two signals respond non-linearly with respect to each other. These techniques are described in WO00/16089 and O'Connor et al., J. Electroanal. Chem. 466(2):197-202 (1999), hereby expressly incorporated by reference."**(Page 97, lines 1-19);** **Pages 10-11, lines 16-21 (above);** **Figures 71-73**
41	**Pages 10-11, lines 16-21 (above);** **Figures 71-73**
42	"In a preferred embodiment, the biochip comprises a substrate with at least one surface comprising an array, and in a preferred embodiment, an array of electrodes. By "electrode" herein is meant a composition, which, when connected to an electronic device, is able to sense a current or charge and convert it to a signal. Alternatively an electrode can be defined as a composition which can apply a potential to and/or pass electrons to or from species in the solution. Thus, an electrode is an ETM as described herein. Preferred electodes are known in the art and include, but are not limited to, certain metals and their oxides, including gold; platinum; palladium; silicon; aluminum; metal oxide electrodes including platinum oxide, titanium oxide, tin oxide, indium tin oxide, palladium oxide, silicon oxide, aluminum oxide, molybdenum oxide (Mo2O6), tungsten oxide (WO3) and ruthenium oxides; and carbon (including glassy carbon electrodes, graphite and carbon paste). Preferred electrodes include gold, silicon, carbon and metal oxide electrodes, with gold being particularly preferred." **(Page 30, lines 11-22);** "There are a variety of techniques that can be used to increase the signal, decrease the noise, or make the signal more obvious or detectable in a background of noise. That is, any technique that can serve to better identify a signal in the background noise may find use in the present invention. These techniques are generally classified in three ways: (1) variations in the type or

methods of applying the initiation signals (i.e. varying the "input" to maximize or identify the sample signal); (2) data processing, i.e. techniques used on the "output" signals to maximize or identify the sample signal; and (3) variations in the assay itself, i.e. to the electrode surface or to the components of the system, that allow for better identification of the sample signal. Thus, for example, suitable "input" AC methods include, but are not limited to, using multiple frequencies; increasing the AC amplitude; the use of square wave ACV; the use of special or complicated waveforms; etc. Similarly, suitable "output" AC techniques include, but are not limited to, monitoring higher harmonic frequencies; phase analysis or filters; background subtration techniques (including but not limited to impedance analysis and the use of signal recognition or peak recognition techniques); digital filtering techniques; bandwidth narrowing techniques (including lock-in detection schemes particularly digital lock in); Fast Fourier Transform (FFT) methods; correlation and/or convolution techniques; signal averaging; spectral analysis; etc. Additionally, varying components of the assay can be done to result in the sample signal and the noise signal being altered in a non-parallel fashion; that is, the two signals respond non-linearly with respect to each other. These techniques are described in WO00/16089 and O'Connor et al., J. Electroanal. Chem. 466(2):197-202 (1999), hereby expressly incorporated by reference.

In general, non-specifically bound label probes/ETMs show differences in impedance (e.g. higher impedances) than when the label probes containing the ETMs are specifically bound in the correct orientation. In a preferred embodiment, the non-specifically bound material is washed away, resulting in an effective impedance of infinity. Thus, AC detection gives several advantages as is generally discussed below, including an increase in sensitivity, and the ability to "filter out" background noise. In particular, changes in impedance (including, for example, bulk impedance) as between non-specific binding of ETM-containing probes and target-specific assay complex formation may be monitored.

Accordingly, when using AC initiation and detection methods, the frequency response of the system changes as a result of the presence of the ETM. By "frequency response" herein is meant a modification of signals as a result of electron transfer between the electrode and the ETM. This modification is different depending on signal frequency. A frequency response includes AC currents at one or more frequencies, phase shifts, DC offset voltages, faradaic impedance, etc.

Once the assay complex including the target sequence and label probe is made, a first input electrical signal is then applied to the system, preferably via at least the sample electrode (containing the complexes of the invention) and the counter electrode, to initiate electron transfer between the electrode and the ETM. Three electrode systems may also be used, with the voltage applied to the reference and working electrodes. The first input signal comprises at least an AC component. The AC component may be of variable amplitude and frequency." **(Pages 97-98, lines 1-4);**

	Pages 10-11, lines 16-21 (above); **Figures 71-73**
43	"While the exact system will vary with the composition of the SAM and the choice of the ETM, in general, the test for a suitable SAM to reduce non-specific binding that also has sufficient electroconduits for ETM detection is to add either ferrocene or ferrocyanide to the SAM; the former should give a signal and the latter should not."**(Page 39, lines 19);** "The choice of the specific ETMs will be influenced by the type of electron transfer detection used, as is generally outlined below. Preferred ETMs are metallocenes, with ferrocene being particularly preferred (Page 69:lines 23-25) **Pages 10-11, lines 16-21 (above);** **Figures 71-73**
44	"Accordingly, in a preferred embodiment, the present invention provides biochips (sometimes referred to herein "chips") that comprise substrates comprising a plurality of electrodes, preferably gold electrodes. The number of electrodes is as outlined for arrays. Each electrode preferably comprises a self-assembled monolayer as outlined herein. In a preferred embodiment, one of the monolayer-forming species comprises a capture ligand as outlined herein. In addition, each electrode has an interconnection, that is attached to the electrode at one end and is ultimately attached to a device that can control the electrode. That is, each electrode is independently addressable." **(Page 31:lines 15-21);** **Pages 10-11, lines 16-21 (above);** **Figures 71-73**
45	"In a preferred embodiment, the detection electrode comprising the SAM (or the sites on the array, for non-electrode embodiments) further comprises capture binding ligands, preferably covalently attached. By "binding ligand" or "binding species" herein is meant a compound that is used to probe for the presence of the target analyte, that will bind to the target analyte. In general, for most of the embodiments described herein, there are at least two binding ligands used per target analyte molecule; a "capture" or "anchor" binding ligand (also referred to herein as a "capture probe", particularly in reference to a nucleic acid binding ligand) that is attached to the detection electrode as described herein, and a soluble binding ligand (frequently referred to herein as a "signaling probe" or a "label probe"), that binds independently to the target analyte, and either directly or indirectly comprises at least one ETM. However, it should be noted that for fluorescence-based nucleic acid detection systems, the target sequence is generally amplified, and during amplification, a fluorescent label is added; thus these systems generally comprise only two elements, the capture probe and the labeled target. Again, the discussion below is directed to the use of electrodes and electrochemical detection, but as will be appreciated by those in the art, fluorescent based systems can be used as well." **(Page 56:lines 10-23);**

	Pages 10-11, lines 16-21 (above); **Figures 71-73**
46	"In a preferred embodiment, the stations of the device include signaling systems. For example, a system of lights, particularly colored lights, at each station can be used to indicate the status of the cartridge or the assay: cartridge present or absent, assay in progress, error, assay completed, etc. In addition, the configuration of the lights may be the code (particularly for color blind people); two lights for cartridge in, flashing lights for assay finished, etc. Again, these signaling systems may be at each station or at sets of stations. In a preferred embodiment, the devices of the invention include an alphanumeric display to allow the display of data or other information." **(Pages 87-88; lines 36-6);** **Pages 10-11, lines 16-21 (above);** **Figures 71-73**
47	**Page 87, lines 4-29 (above);** **Pages 10-11, lines 16-21 (above);** **Figures 71-73**
48	"In a preferred embodiment, each station comprises an individual thermal controller. "Thermal controller" or "thermocontroller" in this context includes elements that can both heat and cool the cartridges and thus the samples in the cartridges as well. In general, given the size and function of the systems, it is desirable to utilize small, fast thermocontrollers. There are a wide variety of known suitable thermocontrollers, including Peltier systems." **(Page 87, lines 8-12);** **Pages 10-11, lines 16-21 (above);** **Figures 71-73**
49	**Page 11, lines 25-34 (above);** **Figures 71-73**
50	**Pages 10-11, lines 16-21 (above);** **Figures 71-73**
51	**multiplexers** "The present invention is directed to devices designed to receive and analyze a plurality of biochips, each comprising an array of biological moieties, such as nucleic acids or proteins, to allow high throughput analysis and detection of target analytes in samples. Thus for example a number of samples (particularly patient samples) can be simultaneously analyzed, or multiple assays can be run on a single sample. The devices comprise a number of cartridge stations that are configured to receive the biochips, with different types of biochips allowing different types of components. The stations can include a wide variety of different components, including thermocontrollers, signaling systems, sensors for leak detection, alphanumeric displays, and detectors. Preferred embodiments include the use of biochips comprising electrodes that rely on electrochemical detection, and thus the devices and/or stations can comprise device boards and processors." **(Page 11, lines 25-34);**

	Pages 10-11, lines 16-21 (above); **<u>thermocontrollers</u>** **Page 11, lines 11-14 (above)** **Figures 71-73**
52	"In Figure 71, there is illustrated a schematic block diagram of an exemplary signal processing approach. A digital to analog converter (DAC) receives a digital signal from a signal source (such as signal generating circuitry on the signal processing printed circuit board or received from a connected personal computer) and converts that signal into an analog signal which is received by filter. The characteristics of filter may be modified to provide frequency low-pass, high-pass, or single or multiple band-pass characteristics according to tailored the signal applied to the electrodes of the E-Chem Cell. In this embodiment, the filtered signal is passed through resistor R9 (110 Kohm) before passing through a first auxiliary amplifier (AUX AMP). To reduce signal complexity and cost, the signal is desirably multiplexed through multiplexer (MUX) and distributed to a plurality of auxiliary electrodes on the E-Chem cell cartridge. A set of reference electrodes is also disposed within the E-Chem Cell cartridge, the outputs of which are coupled to through a second multiplexer (MUX) and reference amplifier (REF AMP) and resistor R13 (110 Kohm) back to the input of first auxiliary amplifier. Finally, a set of active electrodes (36 active electrodes in this embodiment) are coupled via printed circuit board traces to a third mutiplexer. The output of this active electrode multiplexer is amplified by an input signal amplifier (INPUT AMP), and after further optional signal conditioning (such as filtering, gain control and/or selection) is processed through a buffer amplifier (BUFFER AMP) and converted from analog to digital (ADC) form, so that it may be communicated, processed, analyzed, stored or the like in digital form." (**Pages 10 lines 16-36);** **Figure 71**
53	In a preferred embodiment, each station comprises an individual thermal controller. "Thermal controller" or "thermocontroller" in this context includes elements that can both heat and cool the cartridges and thus the samples in the cartridges as well. In general, given the size and function of the systems, it is desirable to utilize small, fast thermocontrollers. There are a wide variety of known suitable thermocontrollers, including Peltier systems." **(Page 87 lines 8-13);** **Pages 10-11, lines 16-21 (above);** **Figures 71-73**

Applicant's respectfully remind the examiner that the test for written description under §112, first paragraph is from the viewpoint of one of skill in the art, and compliance with

§112, first paragraph, requires "sufficient information in the original disclosure to show that the inventor possessed the invention at the time of the original filing." Moba B.V. v. Diamond Automation, Inc., 325 F.3d 1306, 1320-1 (Fed. Cir. 2003) citing Vas-Cath Inc. v. Mahurkar, 935 F.2d 1555, 1561 (Fed. Cir. 1991). Additionally, drawings alone may be sufficient to provide the written description of the invention required by §112, first paragraph. Vas-Cath Inc. v. Mahurkar, 935 F.2d 1555 (Fed. Cir. 1991). Further, it is not necessary that the claimed subject matter be described identically, but the disclosure originally filed must convey to those skilled in the art that applicant had invented the subject matter later claimed. *In re* Wilder, 736 F.2d 1516 (Fed . Cir.1994) citing *In re* Kaslow, 707 F.2d 1366, 1375, (Fed.Cir. 1983).

In view of the forgoing remarks, Applicant's respectfully request reconsideration and withdrawal of the rejection.

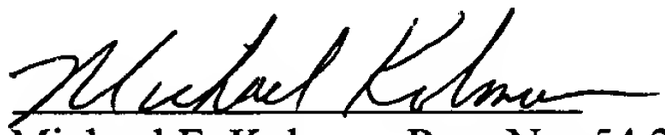
CONCLUSION

Please direct further questions in connection with this petition to the undersigned at (415) 781-1989.

Respectfully submitted,

DORSEY & WHITNEY, LLP

Dated: March 25, 2005

By: 
Michael F. Kolman, Reg. No: 54,234
For Robin M. Silva, Reg. No. 38,304
Filed under 37 C.F.R. §1.34(a)

Customer No.: 32940
Dorsey & Whitney LLP
Four Embarcadero Center, Suite 3400
San Francisco, California 94111-4187
Telephone: (415) 781-1989
Fax No. (415) 398-3249